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EXAMINER	
JUEDES, AMY E	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 09/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/674,433	MATOSSIAN-ROGERS, ARPI	
	Examiner	Art Unit	
	Amy E. Juedes, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,12,14,15 and 17-30* is/are pending in the application.

4a) Of the above claim(s) *1-10,12,14,15 and 17-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/463,158.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of group XI, drawn to a method of treating autoimmune disease with an antibody that binds an anti-TCR Vβ antibody, claims 29 and 30, in the reply filed on 7/8/06 is acknowledged. Applicant has further elected organ specific autoimmune disease as the species of autoimmune disease.

Applicant's traversal is on the grounds that the methods directed to different diseases do not differ with respect to ingredients or methods steps, and additionally are linked by a central disease mechanism. This is not found to be persuasive, since performing the claimed method to treat the different diseases (cancer, cardiovascular disease, and autoimmune diseases) requires different patient populations and results in a different endpoint. Although Applicant asserts that the claimed diseases are linked by a central mechanism (i.e. the presence of hormonal dysregulation, hyperinsulinaemia, or insulin resistance), it is noted that the instant claims encompass treating autoimmune disease, cardiovascular disease, and cancer, which clearly do not share a central disease mechanism. Therefore, the endpoint in treating these divergent diseases would be different. For example, treatment of cancer requires the elimination of tumor cells, which can be accomplished by boosting the host's immune response. In contrast, treating autoimmune disease requires suppressing the host's immune response.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-10, 12, 14-15, 17, and 19-28 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 29-30 read on the elected invention and are being acted upon.

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 29 is indefinite since it does not require that the antibody be administered to the patient with the condition to be treated. For example, it is unclear how a condition can be treated by administering the antibody to a patient without said condition (i.e. "a patient").

B) Claim 29 is indefinite in the recitation of "an effective amount" of the antibody. It is not clear what "effect" is required. For example, are the claims intended to encompass administering an amount effective to be toxic to the patient?

C) Claims 29-30 are indefinite in the recitation of treating a condition where "hormonal dysregulation, hyperinsulinaemia, and/or insulin resistance are present". Specifically, it is unclear how autoimmune diseases, cancer, and cardiovascular disease can be considered conditions where "hormonal dysregulation, hyperinsulinaemia, and/or insulin resistance are present". For example, while some patients with autoimmune disease (for example type 1 diabetics) might have hyperinsulinaemia, it is unclear how all autoimmune diseases (for example, multiple sclerosis) can be classified as a condition where "hormonal dysregulation, hyperinsulinaemia, and/or insulin resistance are present". Multiple sclerosis is well characterized as a T cell mediated autoimmune disease involving an attack on the myelin sheath of the central nervous system. It is unclear how multiple sclerosis can be considered a condition where "hormonal dysregulation, hyperinsulinaemia, and/or insulin resistance are present". Likewise, the recitation of cancer covers a broad range of different diseases. While some types of cancer might involve hormonal dysregulation, hyperinsulinaemia, and/or insulin resistance, it is unclear how, for example, a brain tumor can be considered a condition where "hormonal dysregulation, hyperinsulinaemia, and/or insulin resistance are present".

D) Claim 30 is indefinite in the recitation of "cancer and cancer cachexia". The claim is missing a comma, and is unclear since it is grammatically incorrect.

E)Claim 30 is indefinite in the recitation of the conditions "pre-IDDM" and "pre-NIDDM". The specification does not define the terms, and it is not clear what characterizes a patient as having "pre-IDDM" or "pre-NIDDM". Are the claims intended to encompass treating healthy patients that may or may not develop diabetes?

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 29-30 are rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) A method of treating a condition where "hormonal dysregulation, hyperinsulinaemia and/or insulin resistance are present (Claim 29, and dependant claim 30).

B) A method of treating "pre-IDDM" or "pre-NIDDM" (claim 30).

In the Preliminary Amendments, filed 3/16/06, Applicant indicates that support for the new limitations of Claim 29 can be found at page 29 of the specification, and support for claim 30 can be found in the background information about IDDM and NIDDM at pages 4-6, and page 8.

A review of the specification fails to reveal support for the new limitations.

Regarding A), at page 29, the specification discloses the application of the invention to diseases of hormonal

dysregulation and conditions where hyperinsulinaemia and insulin resistance are present. However, it is noted that the instant claims recite treating conditions where "hormonal dysregulation, hyperinsulinaemia and/or insulin resistance" are present. The specification does not disclose treating a single condition where hormonal dysregulation, hyperinsulinaemia, and insulin resistance are all present, as encompassed by the instant claims. Additionally, the specification does not disclose treating a condition where hyperinsulinaemia alone is present, or where insulin resistance alone is present. The specification only discloses treating conditions where hyperinsulinaemia and insulin resistance are present.

Regarding B), the specification does not disclose treating "pre-IDDM" or "pre-NIDDM". In fact the specification does not disclose the terms "pre-IDDM" or "pre-NIDDM". It is noted that in the remarks accompanying the preliminary amendment, Applicant argues that even though the terms "pre-IDDM" and "pre-NIDDM" are not specifically recited, the detailed description of IDDM and NIDDM includes some discussion of the development of disease, and therefore one of ordinary skill in the art would inherently recognize that the development of IDDM and NIDDM means conditions of "pre-IDDM" and "pre-NIDDM". However, it is noted that obviousness is not the standard for determining new matter, and the specification only discloses treating IDDM or NIDDM and not "pre-IDDM" or "pre-NIDDM", as now claimed.

5. Claims 29-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification provides insufficient evidence that the claimed method could function to treat conditions where hormonal dysregulation, hyperinsulinaemia, and/or insulin resistance are present by administering an antibody capable of binding an anti-T cell receptor Vβ antibody, as broadly claimed.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of

predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. With these teachings in mind, an enabling disclosure, commensurate in scope with the breadth of the claimed invention, is required.

With regards to the instant claims, their breadth comprises a primary issue as regards the unpredictability of the claimed method. The instant method involves administering an antibody which is capable of binding an anti-T cell receptor antibody to treat conditions where hormonal dysregulation, hyperinsulinaemia, and/or insulin resistance are present. It is noted that this encompasses using a wide range of different antibodies. For example, the method might encompass using an antibody that is capable of binding the Fc portion of the anti-T cell receptor antibody. Said Fc binding antibody would bind to virtually any other antibody, in addition to specifically binding to the anti-T cell receptor antibody. It is not clear how said antibodies would be useful for treating all of the various conditions encompassed by the claims. For example, rheumatoid factor (one type of antibody that binds to the Fc portion of an antibody) is well known to be associated with severe rheumatoid arthritis (see Dorner et al. in particular), and would not likely be useful for treating autoimmune diseases such as rheumatoid arthritis. Furthermore, a review of the instant specification reveals that a key aspect of the

antibodies of the instant method involve their ability to also recognize other antigens, such as those expressed by pancreatic alpha cells, in addition to binding an anti-TCR antibody. It is noted that the instant claims in no way require that the antibodies bind any other antigen than the anti-TCR antibody.

Additionally, even if the claims were limited to the cross-reactive antibodies described in the specification (i.e. those that bind with anti-Vβ in addition to phophatidyl inositol, cardiolipin, ds DNA etc.) it is still not clear how the antibodies would be able to treat conditions where hormonal dysregulation, hyperinsulinaemia, and/or insulin resistance are present. The instant specification demonstrates that a particular antibody raised against an anti-TCR antibody binds to alpha cells and modulates insulin secretion. The instant specification states on pg. 36 that the injection of antibody will be designed to prevent the development of autoantibodies of the same specificity by a feedback mechanisms suppressing existing B cells, or by an idiotypic network of antibody development giving rise to protective mechanisms. However, it is noted that the instant specification does not provide any evidence that antibodies specific for an anti-TCR antibody play a pathogenic role in the broad range of conditions encompassed by the claims, and thus it is not clear how preventing the development of such antibodies would be of benefit. For example, the claims encompass in their breadth, not only treating conditions like diabetes, that directly involve an altered insulin response, but encompass treating any condition where "hormonal dysregulation, hyperinsulinaemia, and/or insulin resistance" are present. This might encompass treating menopause, thyroid disease, or even depression. Furthermore, it is noted that dependent claim 30 recites treating autoimmune disease, cancer, or cardiovascular disease, as the condition. Therefore, the claims encompass treating, for example, multiple sclerosis, brain tumors, varicose veins, aneurysm etc. The instant specification does not provide any mechanistic link as to how the insulin modulating properties of the antibodies would correlate with their ability to treat the widely different diseases and conditions encompassed by the claims.

Therefore, given the breadth of the claims and the state of the prior art, the instant specification must provide a sufficient and enabling disclosure, commensurate in scope with the instant claims. The instant specification demonstrates that a particular antibody raised against an anti-TCR antibody binds

to alpha cells and modulates insulin secretion. The specification further demonstrates that antibodies that bind to anti-TCR antibody are present in 3 patients with IDDM. The conclusion drawn by Applicant appears to be that the antibodies play a pathogenic role in IDDM, and that treatment with the same antibodies can function in suppressive feedback mechanism. However, even if administering the antibodies could function to suppress the development of the same antibodies in vivo, the specification does not correlate how this would function to treat the widely divergent diseases encompassed by the claims (i.e. menopause, multiple sclerosis, brain tumors, etc.). Furthermore, even if the claims were limited to treating insulin related disorders such as diabetes, it is noted that Applicant has not provided any evidence that the antibodies found in the IDDM patients are pathogenic. For example, they have not demonstrated that the anti-anti-TCR antibodies present in vivo modulate insulin secretion or bind to alpha cells, or even that the antibodies are selectively present in IDDM patients and not in controls. Furthermore, given the fact that the claimed treatment involves administering the supposed pathogenic antibody, it seems extremely unpredictable as to whether the antibody would be able to function in a suppressive feedback mechanism, as asserted by Applicant, without itself also inhibiting insulin production and exacerbating diabetes. Moreover, the instant specification does not provide any working examples demonstrating the effectiveness of administering the antibodies to treat any disease (including diabetes). Accordingly, the method as broadly claimed must be considered highly unpredictable. Given said unpredictability, the method of the instant claims must be considered to require undue experimentation.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 29-30 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 92/12996 (of record), as evidenced by Pan et al., 1995.

WO 92/12996 teaches a method for treating autoimmune disease (including organ specific autoimmune diseases such as rheumatoid arthritis and multiple sclerosis) by administering an anti-idiotypic antibody having an internal image of a TCR peptide, including a Vβ peptide (see pg. 3, 18, and 20 in particular). As evidenced by Pan et al., anti-idiotypic antibodies are elicited against an antibody, and those that carry an internal image recognize the combining site of the antibody that is in contact with the original antigen (see pg. 43 in particular). In the case of WO 92/12996, the original antigen is the Vβ peptide, and thus the anti-idiotypic antibodies taught by WO 92/12996 bind to the combining site of the antibody that binds to the Vβ peptide (i.e. the anti-idiotypic antibodies bind to an anti-Vβ antibody).

Thus, the reference clearly anticipates the invention.

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, Ph.D. whose telephone number is 571-272-4471. The examiner can normally be reached on 8am - 5pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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9/5/06
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